REMARKS/ARGUMENTS

Claims 13-36 are pending in the application.

The examiner has withdrawn the prior art rejection of claims 13-16 and 25-28 under 35 U.S.C. § 102(e), as being anticipated by Jordan (US 6,017,699).

Claims 13, 17-25 and 29-36 remain rejected under 35 U.S.C. 103(a), as being unpatentable over Mathies et al. and Ruano in view of Rao and further in view of Ahern.

Claims 14-16 and 26-28 are objected to.

In view of the claim amendments above and arguments presented below, Applicant believes that the rejections have been overcome and respectfully requests reconsideration of the application, withdrawal of the rejections, and allowance of the claims.

Summary of Invention

The present invention is generally directed to a kit consisting of a single reaction vessel for each region of the DNA to be sequenced, where each reaction vessel contains sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand of the region of DNA to be sequenced. The sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand are also labeled with a distinguishable detectable label.

The kits of the present invention are made possible as a result of methods and systems that have been previously been determined by the United States Patent and Trademark Office to be patentable (see, e.g., U.S. Patent Nos. 5,789,168; 5,830,657; 5,888,736; 6,083,699; and 6,214,555, to which patents the present application claims priority). The above-referenced patents describe and claim methods and systems for simultaneous PCR amplification and direct sequencing of multiple target DNAs, a methodology now commonly referred to as "CLIP sequencing." CLIP sequencing is essentially a patentable improvement on the coupled amplification and sequencing method of Ruano et al., in that CLIP sequencing (1) utilizes an improved engineered mutant of thermostable DNA polymerase that lacks 5′-3′ exonuclease activity that is capable of incorporating chain terminating dideoxynucleotides into an extending nucleic acid polymer at higher rates relative to the rate of incorporation of deoxynucleotides,

thereby producing uniform band intensities, and (2) utilizes two inward-facing primers having distinguishable detectable labels to generate sequencing fragments for the sense and anti-sense DNA strands. Consequently, CLIP sequencing can be used to simultaneously amplify and sequencing substantially natural abundance DNA, and represents a novel methodology that enables and provides utility to kits that combine multiple primers, one specific for the sense strand of DNA and the other for the anti-sense strand of DNA, in a single reaction vessel, for obtaining bi-directional sequence of a target region of DNA. The kits of the present invention are therefore useful for diagnostic sequencing of DNA samples, and reduce risk of error and contamination, increase the ease with which the procedure can be automated, and thereby potentially decrease the marginal costs in terms of equipment and labor for performing the test, as well as increase the reliability and accuracy of such tests.

Claim Rejection Under 35 USC § 103

The only remaining rejection is the prior art rejection of claims 13, 17-25 and 29-36 under 35 U.S.C. § 103(a) as being unpatentable over Mathies et al. (U.S. Patent No. 5,707,804) and Ruano (U.S. Patent No. 5,427,911) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14 (1994)) and further in view of Ahern (The Scientist, Vol. 9, No. 15, pages 1-15 (June 1995)). The examiner explains that although the prior art references teach primers for copying a single stranded nucleic acid, the claims are broadly written "with intended use limitations" and "do not recite any structural properties or features of the claimed product which distinguishes it over the prior art." The examiner further notes that the MPEP states that

> "a recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim."
>
> "language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation."

The Examiner argues that the claim limitations "for each DNA region to be sequenced" and "for sequencing sense and antisense strands" constitute intended use limitations that do not provide structural features. The Examiner then interprets the claim as being limited solely to "a kit comprising a single reaction vessel containing a mixture of region specific sequencing reagents,

wherein said region-specific reagents comprises region-specific primers." Based on this claim construction (which effectively eliminates and ignores claim limitations essential to the subject matter of the invention), the examiner concludes that the teaching of Mathies of "primers for copying a single stranded nucleic acid" (column 14, lines 12-26, claim 8, which) meets the claim limitation of "region-specific sequencing reagents, wherein said region-specific reagents comprises region-specific primers."

Applicant traverses this rejection on grounds that the rejection improperly ignores claim limitations that require the kits to contain sequencing primers for both the sense and anti-sense strands of the target region of interest, and therefore fails to compare the prior art with all of the limitations of the claims. As noted above, the Examiner has rejected the claims based on a claim construction that effectively limits the claim to "a kit comprising a single reaction vessel containing a mixture of region specific sequencing reagents, wherein said region-specific reagents comprises region-specific primers," which claim construction completely ignores the claim language underlined in claim 13 below:

> 13. A kit for sequencing one or more DNA regions from a genomic DNA sample or a microorganism, said kit consisting of, in packaged combination, a single reaction vessel for each DNA region to be sequenced containing a mixture of region-specific sequencing reagents sufficient for sequencing the sense and anti-sense strand of each DNA region to be sequenced and optionally in said mixture one or more non-region specific sequencing reagents, wherein said region-specific sequencing reagents comprise region-specific primers, and said optional non-region specific sequencing reagents are selected from one or more of the group consisting of deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer.

Applicant respectfully submits that the above construction of the claim (which ignores the underlined portions) is in error. In particular, Applicant submits that the phrase "region-specific sequencing reagents sufficient for sequencing the sense and anti-sense strand of each DNA region to be sequenced" constitutes a limitation that inherently requires structural elements of region-specific primers for both the sense and anti-sense strands. Without primers for both the sense and anti-sense strands, the recited function of "sequencing the sense and anti-sense strand of each DNA region" could not be accomplished. Therefore, the functional language of claim 14 does in fact require the necessary structural limitations. The teaching of Mathies of a single primer for copying a single stranded nucleic acid cannot meet the limitation that it is "sufficient

for sequencing the sense and anti-sense strand of each DNA region to be sequenced." For this reason, Applicant submits that the claims are patentably distinct from the cited prior art.

Notwithstanding the fact that claim 13 is believed to inherently require primers specific for both the sense and anti-sense strands of a target DNA region, Applicant has canceled claim 13 and incorporated the contents of claim 13 into claim 14, which now expressly recites the elements of "sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand, wherein said sequencing primers flank the DNA region to be sequenced." The cancellation of claim 13 therefore overcomes the §103 rejection of not only claim 13, but also claims 17-25 and 29-36, which depend directly or indirectly from claim 13.

Objections

The examiner has also objected to claims 14-16 and 26-28. Although no explanation is provided in the final office action of the grounds for the objection, the examiner explained in a telephone conference conducted with the undersigned attorney on April 20, 2006, that the ground of the objection was that the claims are dependent on a rejected base claim. The examiner further indicated that the ground of the objection could be overcome by amending the objected claims to incorporate the limitations of the independent base claim on which the claims depend.

Applicant first traverses the objection to claims 14-16 and 26-28 on grounds that the objection was defective in that it did not provide applicant with any explanation of the grounds of the objection. Applicant respectfully submits that in the absence of any explanation of the basis of the objection, the finality of the office action is premature and should therefore (in the absence of an allowance) be withdrawn. Although the ground of the objection was later explained in the above-referenced telephone conference, Applicant raises this issue in the present response solely for the purpose of preserving this issue for review in the event an appeal is filed.

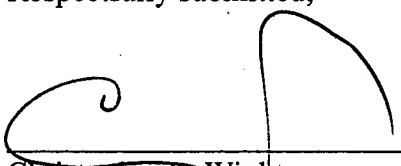
As noted above, the examiner explained in a telephone interview that that the objection was based on the fact that the claims are dependent on a rejected base claim, and that the objection could be overcome by amending the objected claims to incorporate the limitations of the independent base claim on which it depends. Applicant has accordingly amended claim 14 to incorporate all of the limitations of the base claim (claim 13) from which it depends. Amended

claim 14 therefore specifically recites all of the elements of claim 13, and also recites the structural elements of "sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand, wherein said sequencing primers flank the DNA region to be sequenced." In view of the cancellation of claim 13 and the amendment of claim 14, Applicant has also amended claim 25 to change the dependency from claim 13 to claim 14, and cancelled claim 26, the subject matter of which is redundant in view of the dependency of claim 25 on claim 14. The merger of claims 13 and 14 into a single independent claim, and the respective amendments to claims 25, 27 and 28, therefore overcome the grounds of the objection with respect to claims 14-16 and 27-28. Claims 14-16 and 26-28 are no longer subject to any objection or rejection, and are now in condition for allowance.

In summary, Applicant has cancelled claim 13, thereby overcoming the prior art *rejection* under 35 U.S.C. § 103(a) of claim 13, as well as the rejection of dependent claims 17-25 and 29-36. Applicant has also incorporated all of the limitations of claim 13 into claim 14, thereby overcoming the basis of the *objection* of claim 14, as well as claims 15-16 and 27-28. In view of the above amendments and remarks, Applicant respectfully submits that claim 14, from which all other claims depend, now expressly recites the necessary structure to distinguish the claimed invention from the cited prior art.

Claims 14-16 and 26-28 are therefore in condition for allowance, and Applicant therefore requests that the outstanding rejections based on these references be withdrawn, and the claims allowed.

Respectfully submitted,



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